

Magnetic Resonance Imaging: 2018 Updates from The MRI Institute for Biomedical Research

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Disclosure

I am an employee of
Magnetic Resonance Innovations, Inc.

Collaborators

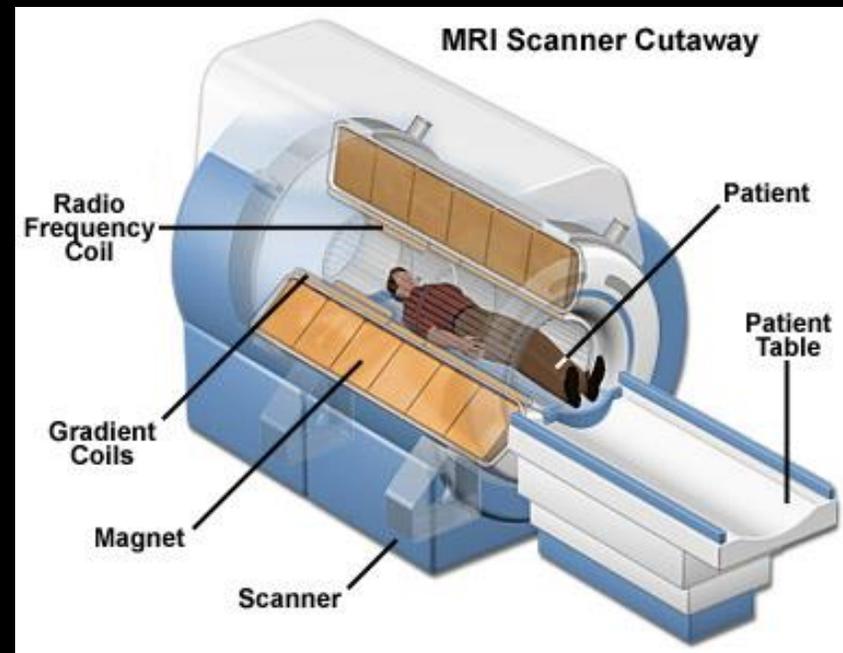
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Outline

- Imaging methods used to visualize and assess MS Lesions
- What can we say from MR data about MS lesion development?
- Demyelination versus inflammation
- Strategically Acquired Gradient Echo – STAGE Imaging
- Cerebral Microbleeds and Calcifications – pSWIM and mpSWIM

Magnetic Resonance Imaging

- Imaging of Water protons in various physical states
- Imaging of Magnetization of diamagnetic and paramagnetic objects



Multiple Sclerosis

MS is a neurodegenerative disease characterized by:

- a wide range of symptoms with multiple progressive disease courses
- self-targeting/autoimmune responses
- venocentric lesions and vascular dysfunction
- destruction and scarring of the myelin sheaths of the central nervous system

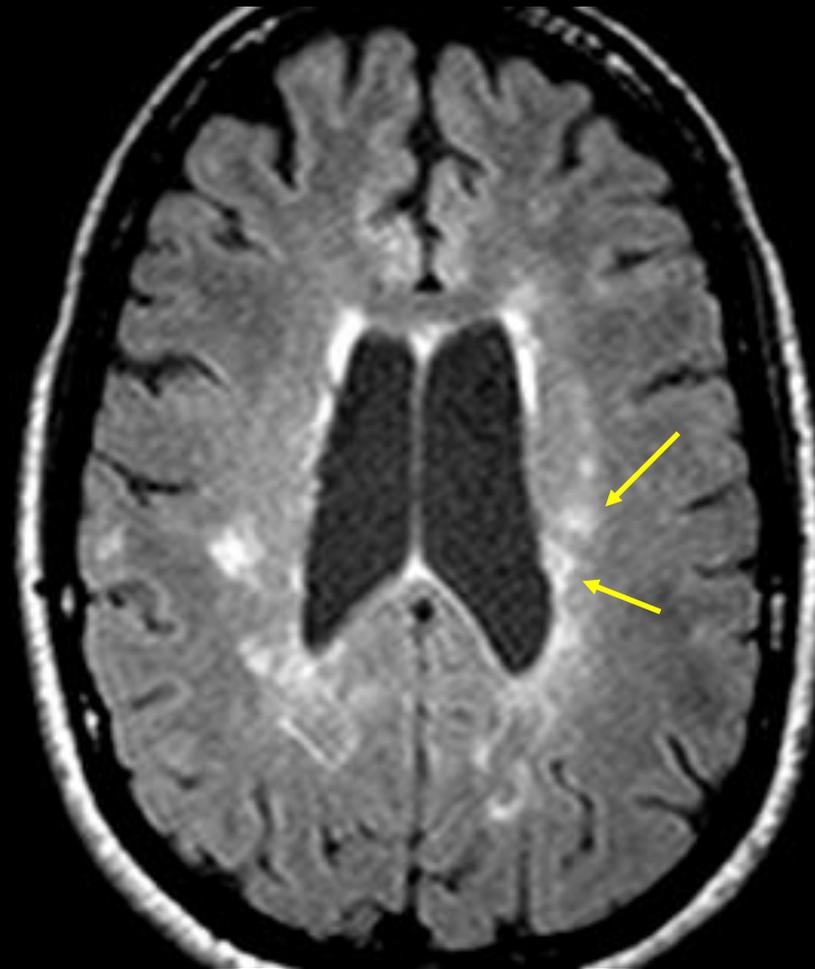
There are many contrasts available in MRI to study white matter and MS lesions.

- Conventional imaging: Pre/Post Contrast T1W, T2W, T2 FLAIR, DWI
- Susceptibility Weighted Imaging (SWI)
- Diffusion Tensor Imaging (DTI)
- Magnetization Transfer Ratio (MTR)
- Perfusion Weighted Imaging (PWI)
- Myelin Water Fraction (MWF)
- STAGE Imaging (for T1 and spin density maps)

T2 Weighted Imaging of MS Lesions

T2 FLAIR

T2 provides excellent contrast to visualize MS lesions, but can it differentiate between the changes from water content and changes in iron content?



T2 Weighted Imaging MS lesions

- The problem with T2W images is that there are two competing processes: high water causing an increase in signal and iron causing a decrease.
 - Recent results suggest there are changes in T2 throughout the brain and possibly changes in T1 reflecting oxidative stress. New methods of quantifying T1 such as STAGE may help characterize these tissue changes earlier and allow for better treatment.
 - One group (1) found that T2 hypointensities seen in gray matter could be linked to physical disability, cognitive dysfunction, and brain atrophy and that they may be caused by increased brain iron content.
 - A recent study showed that even in CIS, T2 relaxometry reveals a non-uniform increase in T2 in cortical gray matter leading to an increase in standard deviation of the signal as well (2).
1. Neema M et al T1- and T2-based MRI measures of diffuse gray matter and white matter damage in patients with multiple sclerosis. *Journal of neuroimaging* 2007;17 Suppl 1:16S-21S.
 2. Gracien RM, Reitz SC, Hof SM, et al. Assessment of cortical damage in early multiple sclerosis with quantitative T2 relaxometry. *NMR in biomedicine* 2016;29(4):444-450.

Susceptibility Weighted Imaging (SWI)

Fully flow compensated 3D gradient echo sequence which combines phase with the T2*W magnitude images for increased contrast.

Using phase and susceptibility, iron and calcium content in tissue can be calculated.

SWI exploits magnetic susceptibility differences between tissues

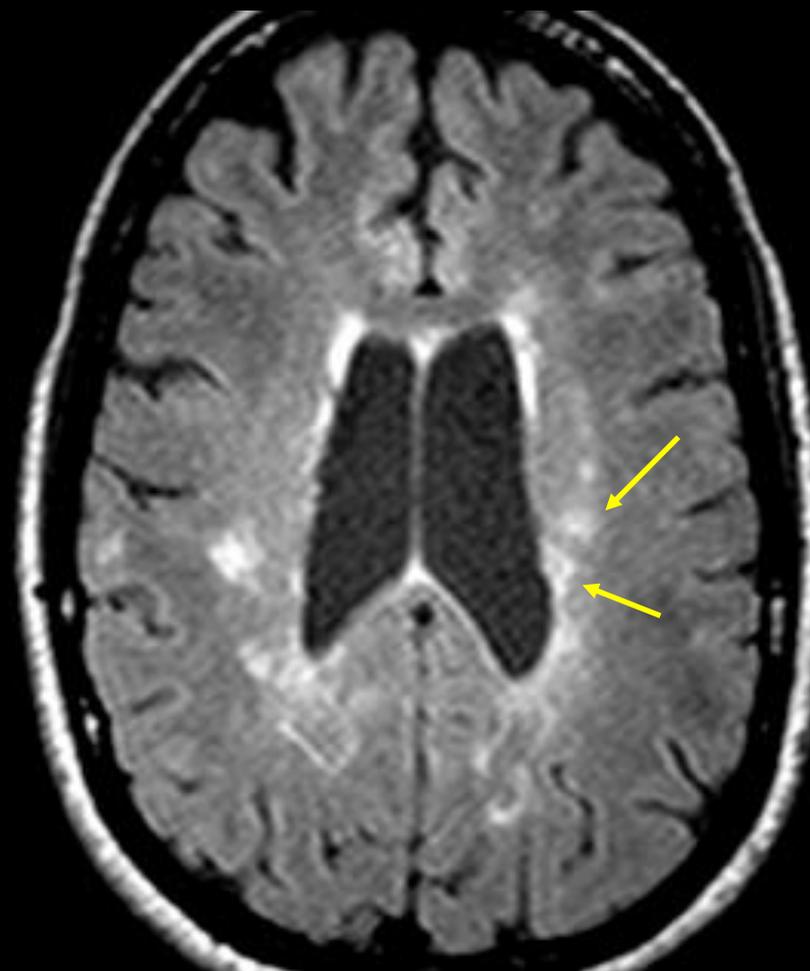
- Deoxyhemoglobin in veins acts as an intrinsic contrast.
- Cerebral microbleeds and venous thrombosis seen in AD, MS, stroke, & TBI.
- Iron deposition in basal ganglia and midbrain can be quantified.
- **Susceptibility changes in MS demyelinated lesions can be seen.**

Venocentric Lesions and Phase Visible Lesions

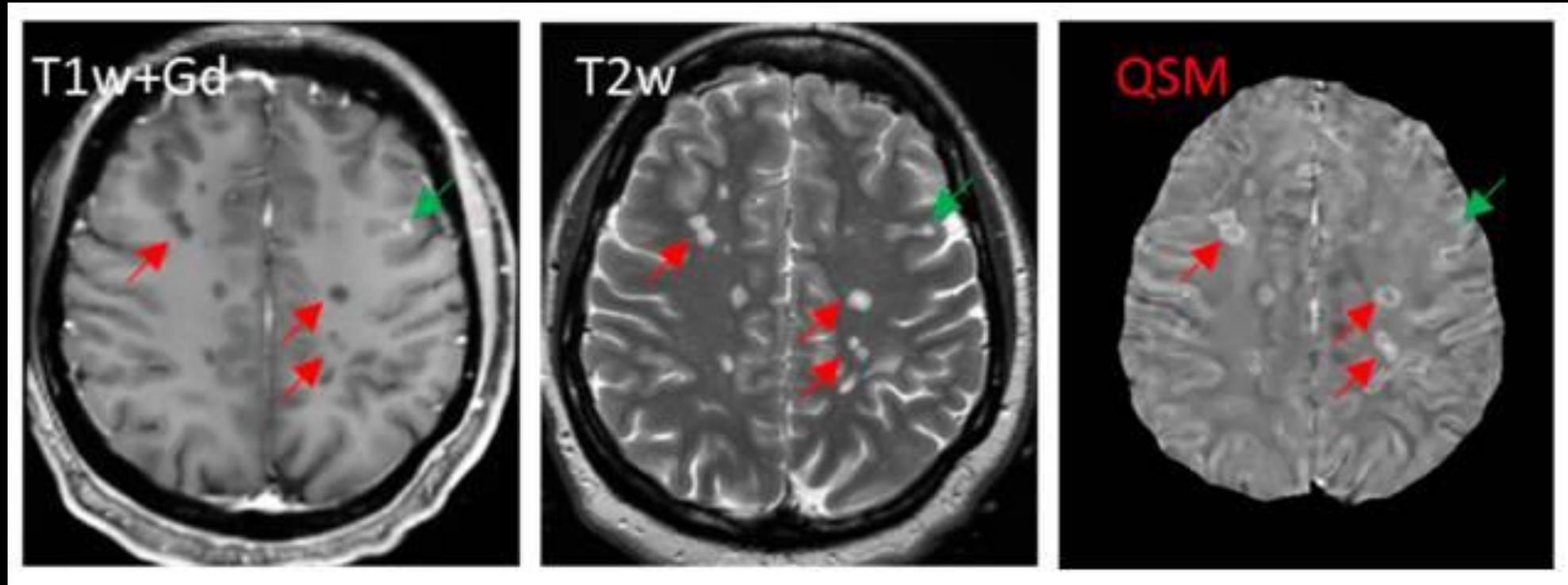
SWI filtered phase



T2 FLAIR



Visualization of MS Lesions with QSM



Non-enhancing lesions appear larger with hyperintense rim on QSM (red arrows) than on T2w, while enhancing lesions appear isointense on QSM (green arrow).

10. Stuber et al. Iron in Multiple Sclerosis and Its Noninvasive Imaging with Quantitative Susceptibility Mapping. *Int J Mol Sci.* 2016 Jan; 17(1):100.

Demyelination vs Inflammation

- A key issue is determining if there is inflammation, demyelination, or both occurring in the lesion.
- The ability to quantitatively determine one versus the other would allow for the appropriate choice of treatment.

Imaging Demyelinating Lesions

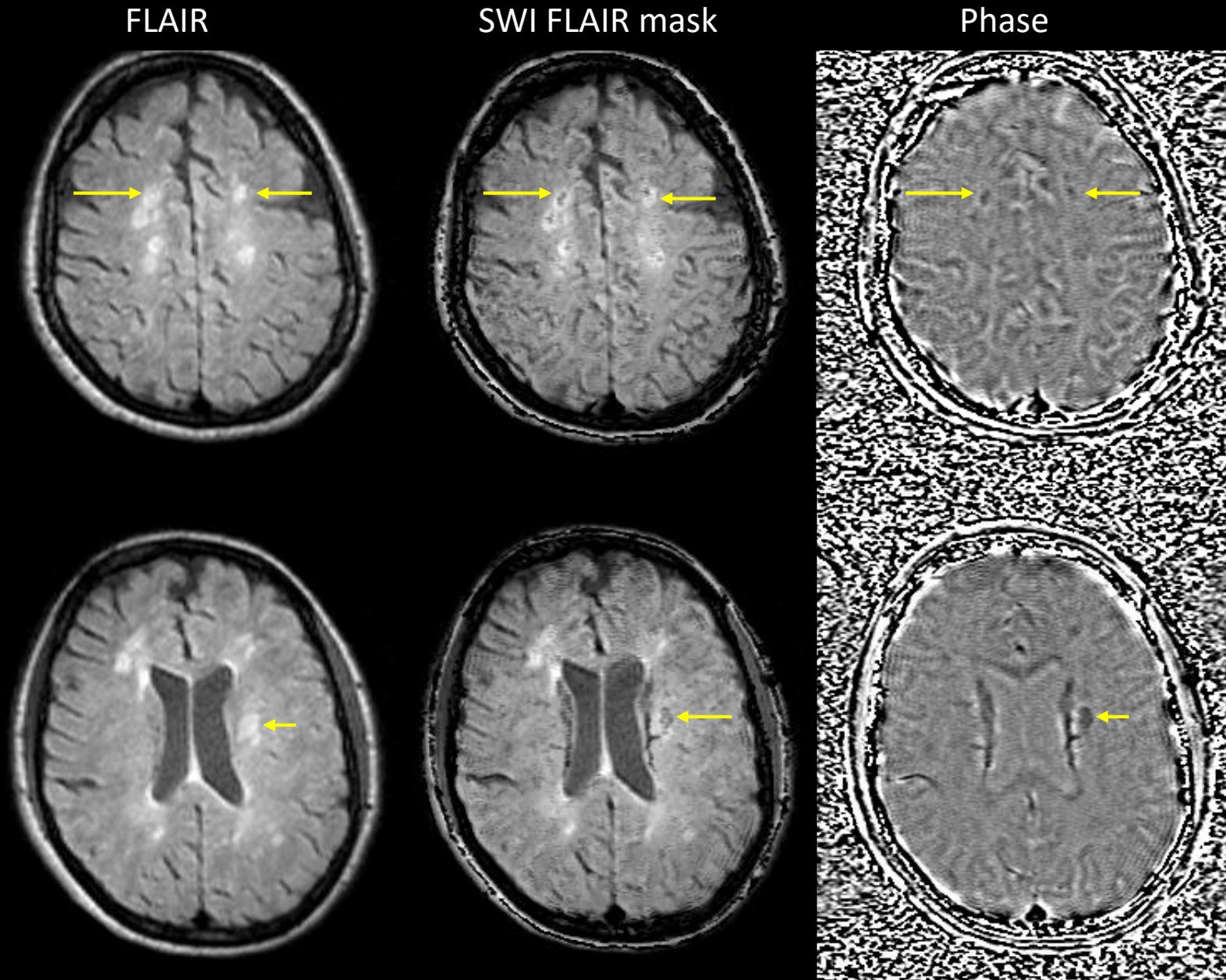
- The myelin sheath of white matter becomes degraded with disease progression.
- The diamagnetic nature of myelin makes the white matter appear to have less iron than gray matter despite the fact that the iron content of each is equal.
- Susceptibility can reveal either demyelination or iron content changes including hypoxia, macrophage iron uptake or iron loss due to cellular degeneration.
- Susceptibility changes during demyelination are up to roughly 50-60ppb.
- Susceptibility changes from iron in macrophages (present in ring lesions for example) can be higher than 60ppb.

FLAIR-SWI

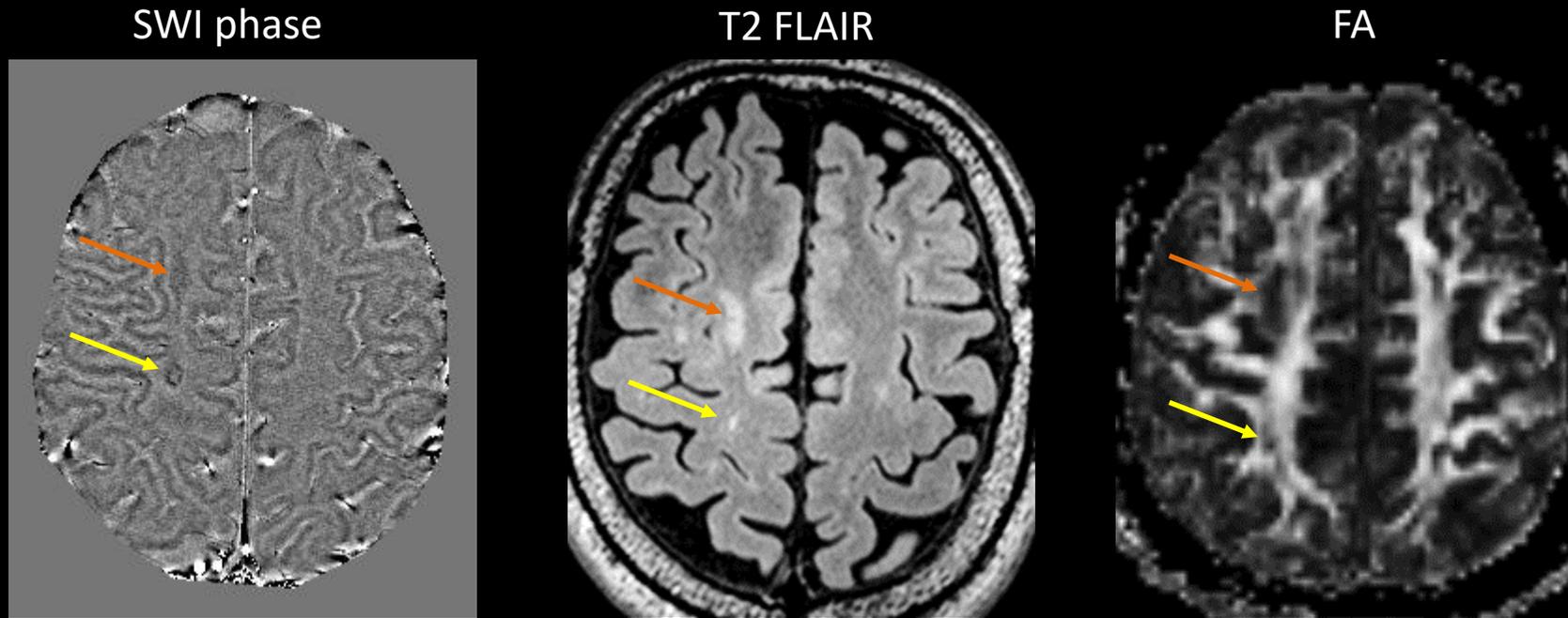
Note that the FLAIR-SWI image has dark regions where there is putative demyelination.

Where there are no black holes in the lesions, this may be early stage inflammation only without demyelination.

That is our hypothesis.



Demyelinated Lesions and Expanding Ring Lesions



- Yellow Arrow – Ring lesion extending to the periphery of a small T2 FLAIR white matter hyperintensity (WMH).
- Do susceptibility changes occur before WMH expansion?
- Orange Arrow – Large demyelinated and inflammatory MS lesion.

Phase and SWI measures of MS lesions

- One study noted the lack of change in phase rim lesions over time (3).
- Another study observed that the phase ring lesions which persist in intensity tend to become more hypointense over time and they may indicate tissue which fails to repair or regenerate itself (4).
- In an experimental autoimmune encephalomyelitis mouse model, SWI phase lesions also matched regions of hypoxia, inflammation, iron deposition, and demyelination (5).

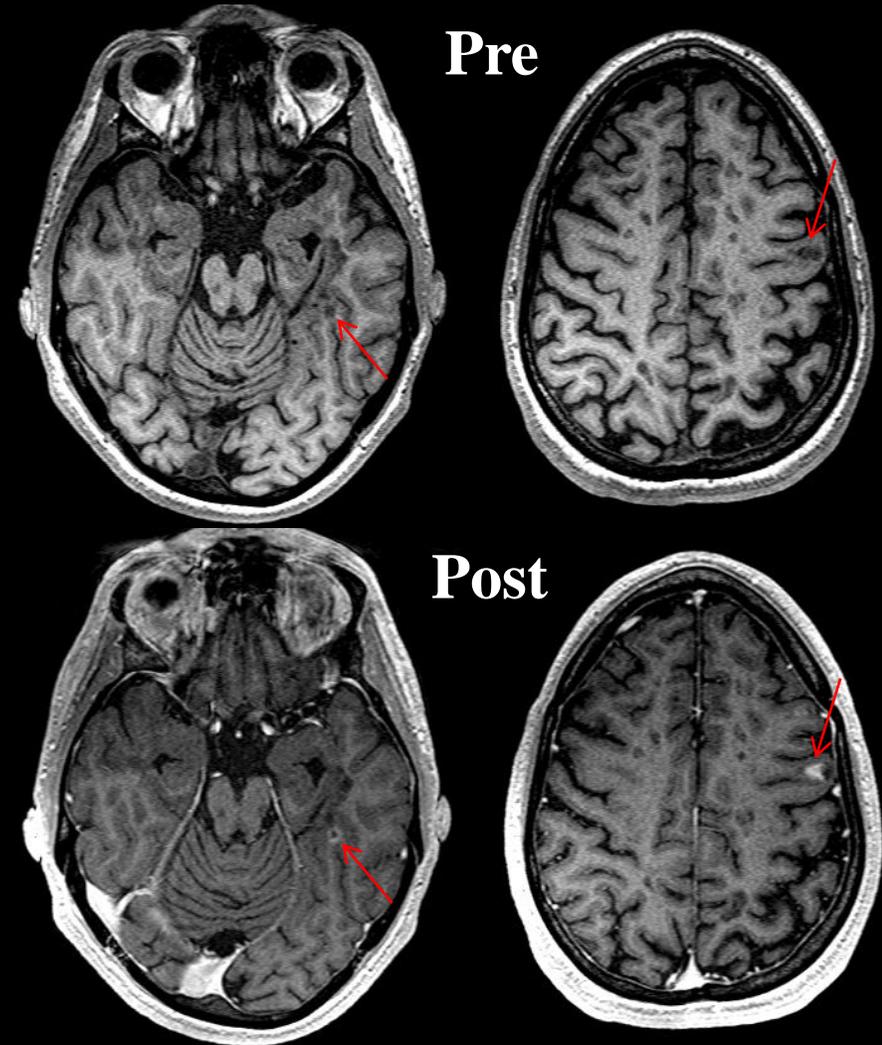
3. Bian W et al. A serial in vivo 7T magnetic resonance phase imaging study of white matter lesions in multiple sclerosis. *Mult Scler* 2013;19(1):69-75.
4. Absinta M et al. Persistent 7-tesla phase rim predicts poor outcome in new multiple sclerosis patient lesions. *J Clin Invest* 2016;126(7):2597-2609.
5. Nathoo N et al. SWI in the experimental autoimmune encephalomyelitis model of multiple sclerosis indicates elevated deoxyhemoglobin, iron deposition and demyelination. *Mult Scler* 2013;19(6):721-731.

Acute Vs Chronic Lesions

- A second issue is differentiating acute vs. chronic lesions.
- BBB contrast leakage as well as increased cerebral blood volume (CBV) may help in that differentiation.

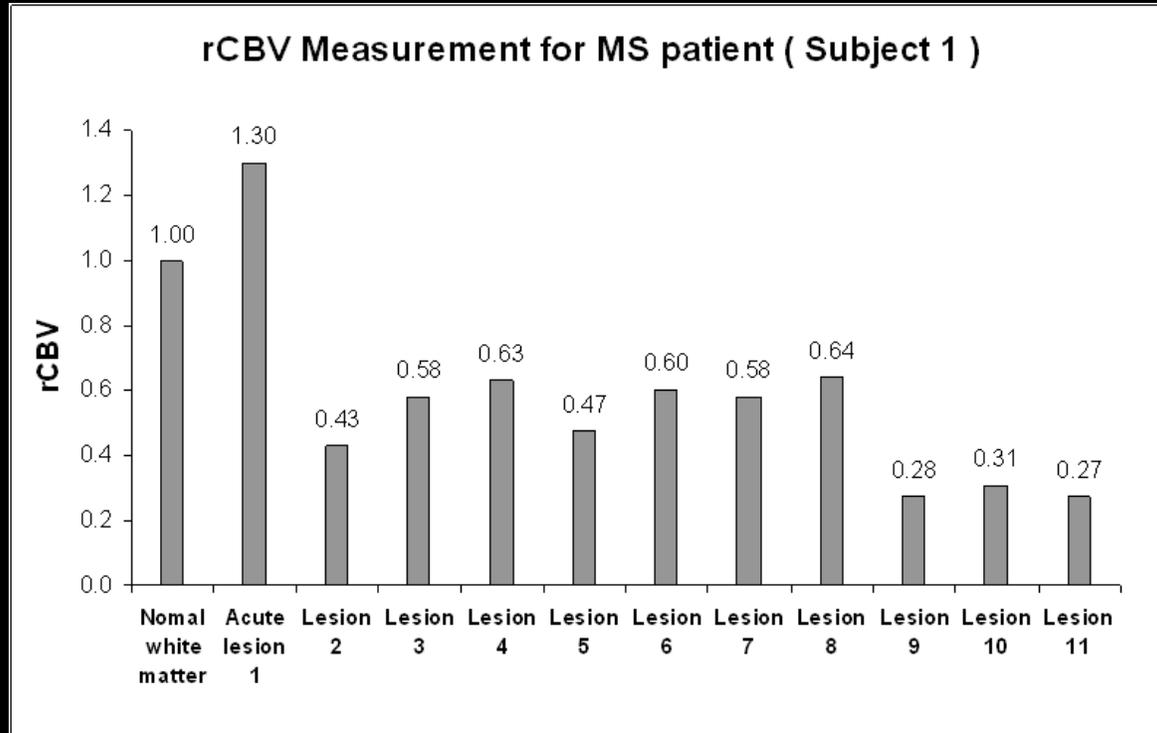
Blood Brain Barrier Breakdown

- Images from a secondary progressive MS patient.
- Pre-contrast T1W show hypo-intense lesions which enhance after contrast injection. These indicate an acute disruption of the BBB.

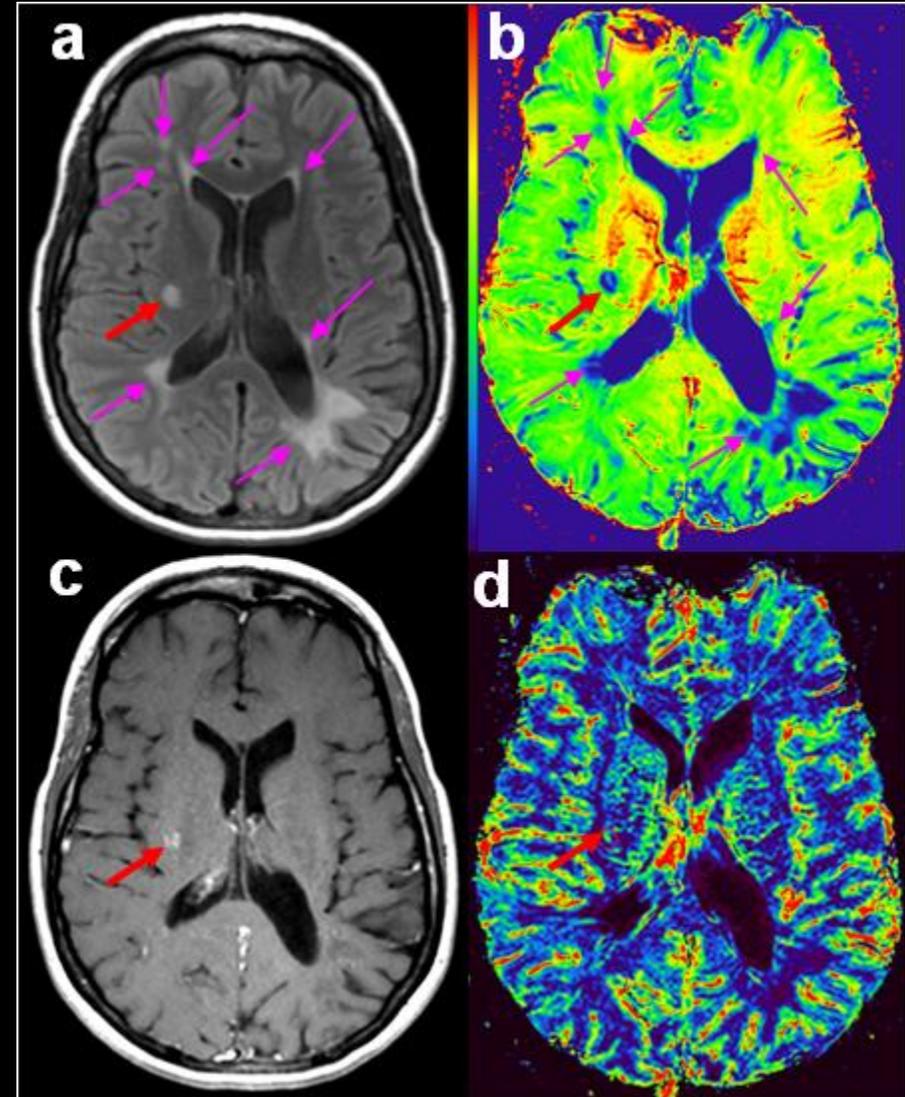


Acute Vs Chronic Lesions

- Acute lesions show higher CBV while chronic lesions show lower CBV.



a) T2 FLAIR, b) TSM, c) Post Contrast T1WI, d) CBV

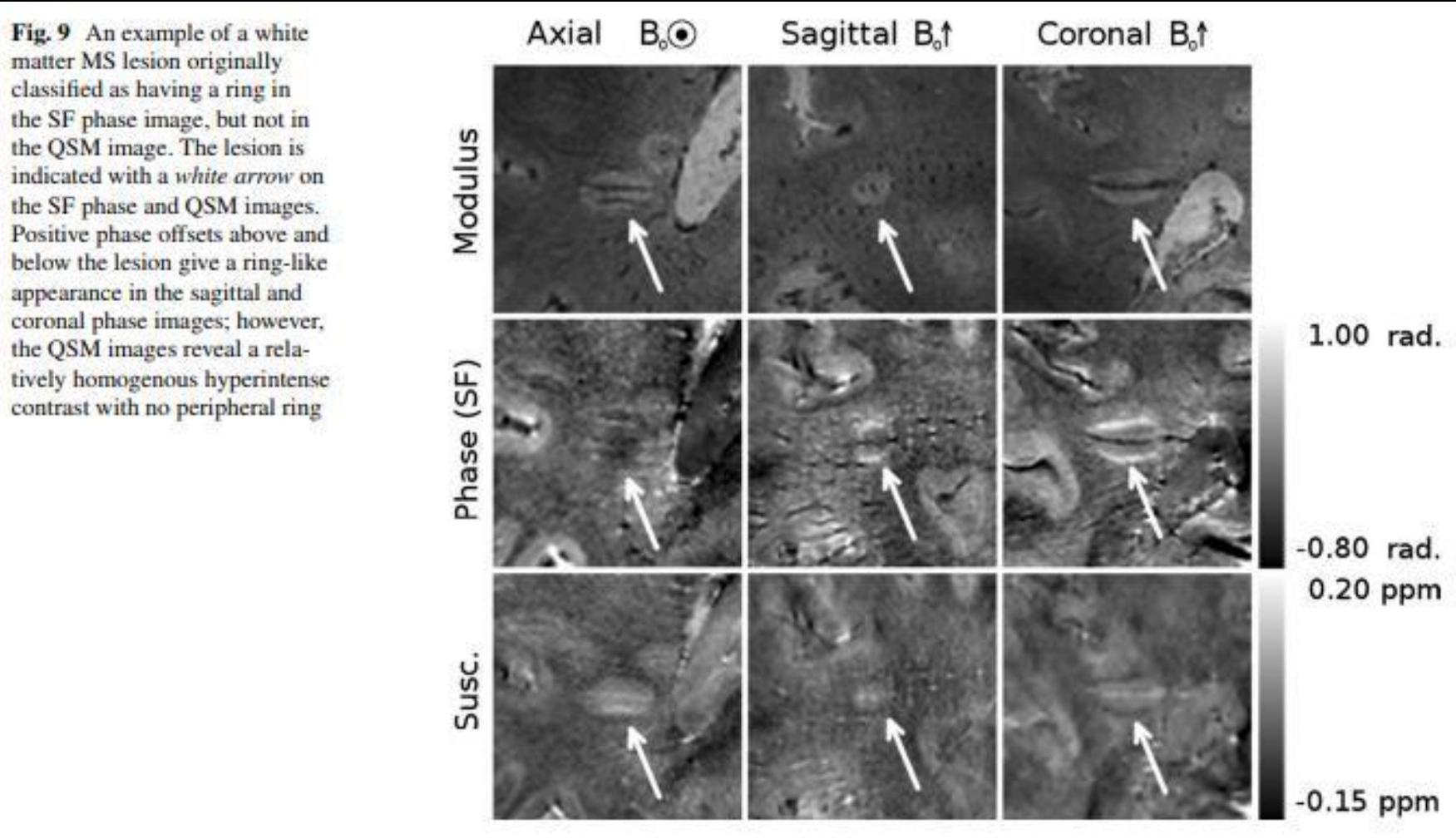


T2* and QSM in studying MS lesions

- T₂* images show both focal intracortical and leukocortical lesions suggesting that perhaps both myelin and iron loss occur (6).
- Early lesion inflammatory responses can be seen with T₂*, while QSM changes were not observed until the chronic phase (7).
- This likely indicates that the tissue T₂* and QSM responses are complicated by the degree of inflammation and changes in iron content and myelin.
- QSM has been shown to improve the accuracy of MS lesion shape and iron content compared to phase imaging (8).

6. Louapre C et al. Beyond focal cortical lesions in MS: An in vivo quantitative and spatial imaging study at 7T. *Neurology* 2015;85(19):1702-1709.
7. Zhang Y et al. QSM and R2* Measured Changes during White Matter Lesion Development in Multiple Sclerosis: Myelin Breakdown, Myelin Debris Degradation and Removal, and Iron Accumulation. *AJNR* 2016;37(9):1629-1635.
8. Cronin MJ et al. A comparison of phase imaging and quantitative susceptibility mapping in the imaging of multiple sclerosis lesions at ultrahigh field. *MAGMA* 2016;29(3):543-557.

QSM Accurately Depicts the Venocentric Nature and Loss of Myelin in MS Lesions



8. Cronin MJ et al. A comparison of phase imaging and quantitative susceptibility mapping in the imaging of multiple sclerosis lesions at ultrahigh field. *MAGMA* 2016;29(3):543-557.

Susceptibility Change in QSM as Myelin is Digested

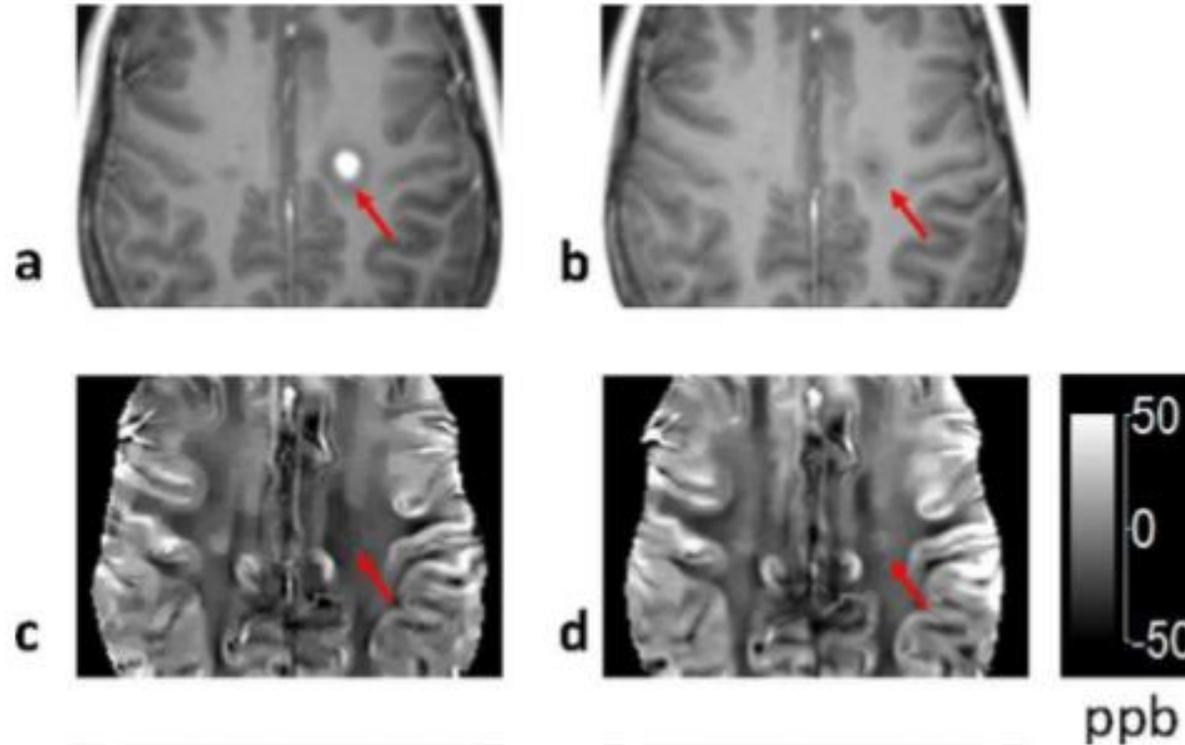


FIGURE 4: Gd enhanced T₁-weighted images (a,b) and corresponding QSM (c,d) of a new acute MS lesion acquired at the time of Gd enhancing (a,c) and 19 days later (b,d). The BBB is closed as evidenced by the nonenhancing appearance in (b). Notice the increase in susceptibility within the lesion (arrow), suggesting myelin digestion by macrophages.

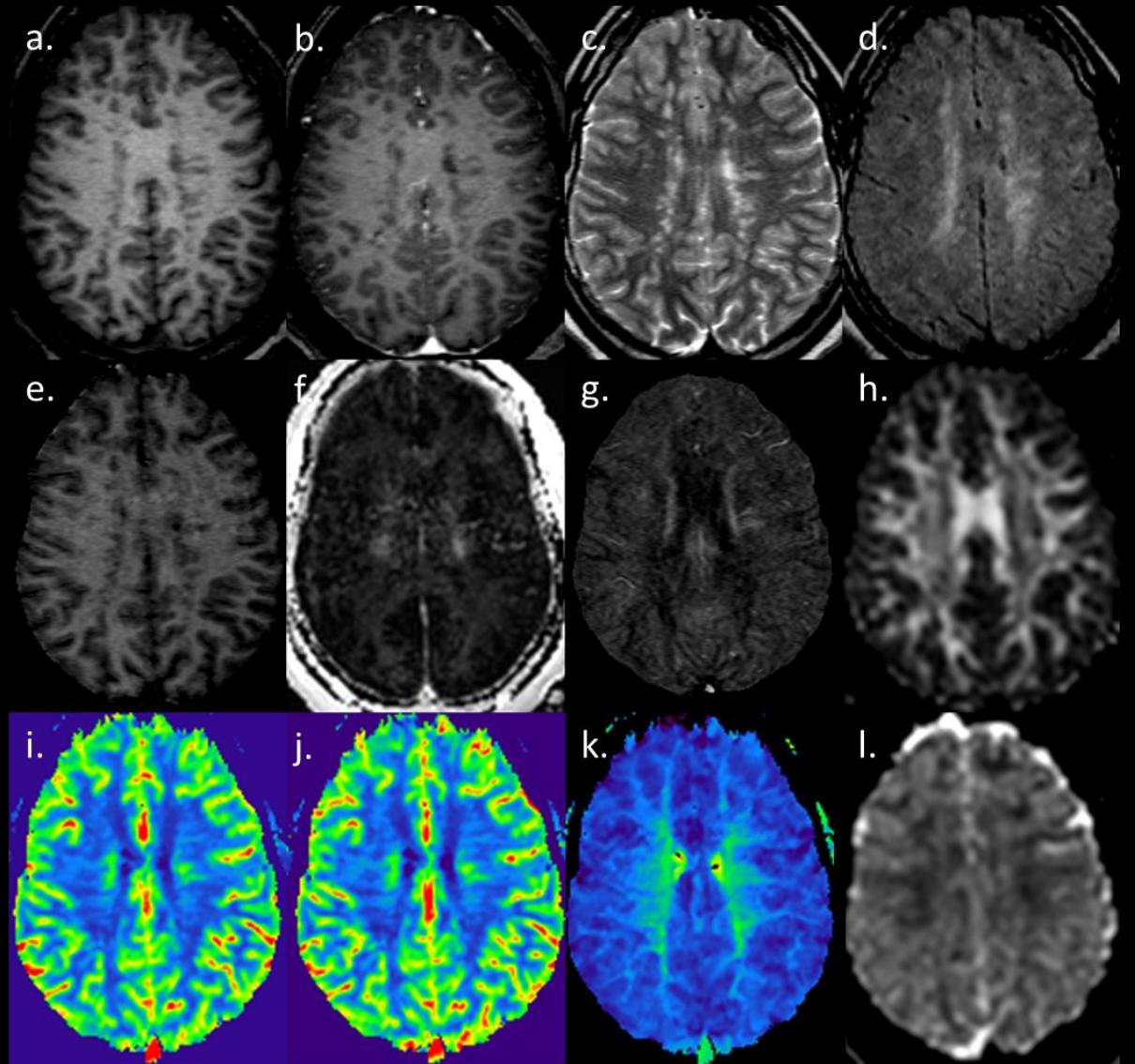
10. Deh et al. Magnetic Susceptibility Increases as Diamagnetic Molecules Breakdown: Myelin Digestion During Multiple Sclerosis Lesion Formation Contributes to Increase on QSM. JMRI 2018; epub ahead of print.

Conclusions

- Various imaging methods have been shown to be sensitive to either demyelination (such as QSM and MWF) or to inflammation (T2 and FLAIR).
- Small changes in susceptibility between zero to 60ppb may be an indication of demyelination separate from inflammation.
- Combining SWI and FLAIR may make it possible to differentiate inflammatory versus demyelinating or inflammatory and demyelinating lesions.
- Being able to differentiate demyelination from inflammation could affect the choice of treatment in MS patients.

Lesion Appearance

- a. pre contrast T1W
- b. post contrast T1W
- c. T2W
- d. T2 FLAIR
- e. MTR – Magnetization Transfer
- f. MWF – Myelin Water Fraction
- g. QSM – Quantitative Susceptibility Mapping
- h. FA – Fractional Anisotropy
- i. CBV – Cerebral Blood Volume
- j. CBF – Cerebral Blood Flow
- k. MTT – Mean Transit Time
- l. ADC – Apparent Diffusion Coefficient



Introduction to STAGE

STAGE provides a practical solution for studying neurodegenerative diseases and gives

8 qualitative and

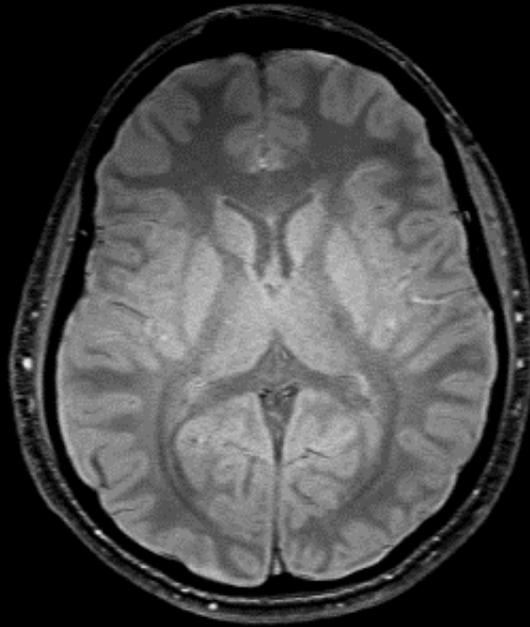
7 quantitative images

within 5 minutes scanning time and

adding T2 FLAIR/DWI in less than 10 minutes.

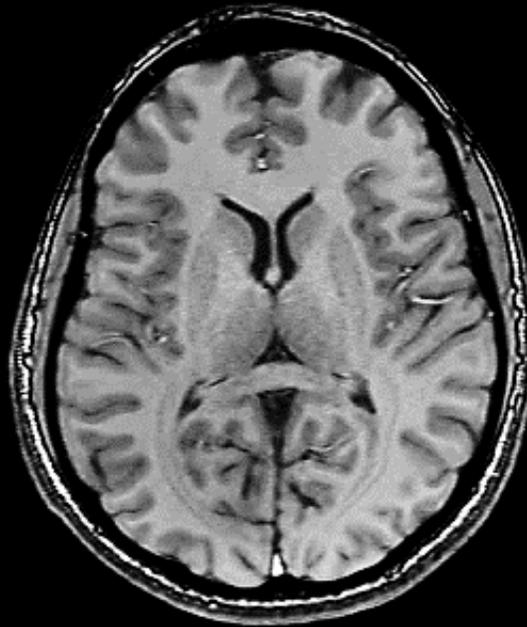
Strategically Acquired Gradient Echo (STAGE) Imaging

SPIN DENSITY WEIGHTED



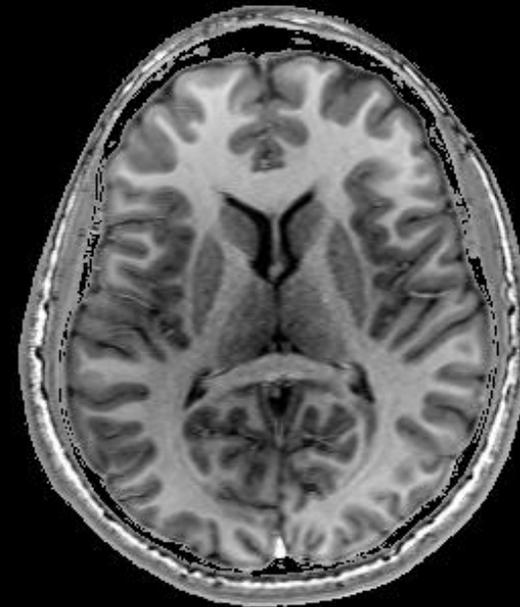
A: FA=6°, TE=7.5

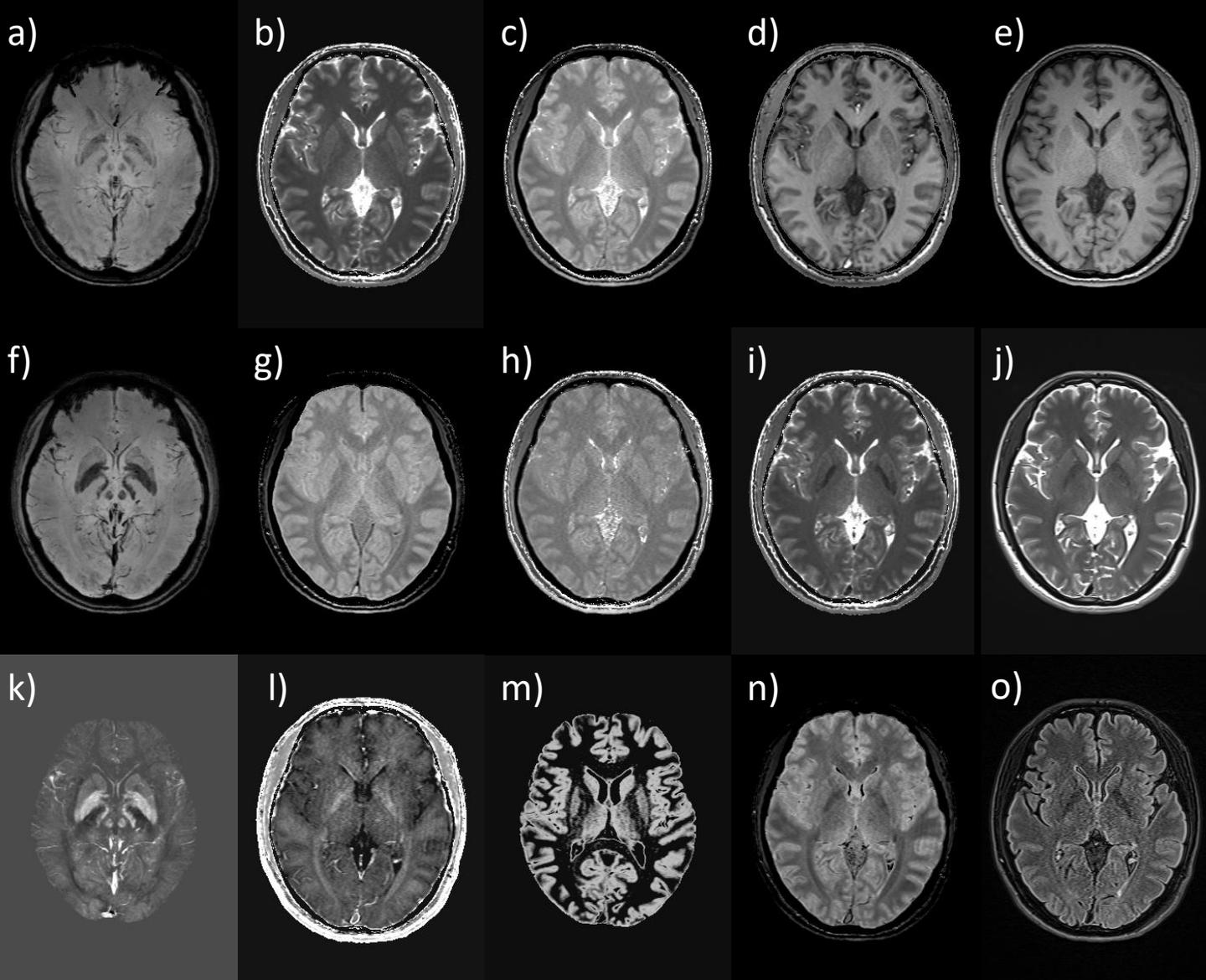
T1 WEIGHTED



B: FA=24°, TE=8.75

STAGE ENHANCED T1W



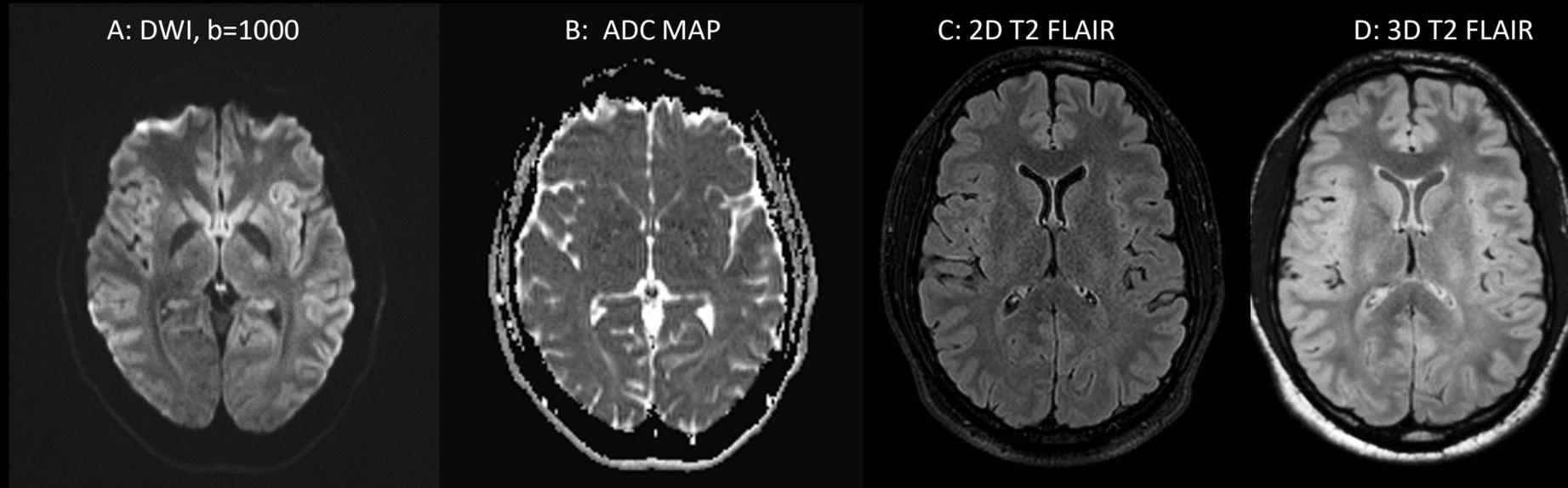


STAGE in
5 minutes

resolution
0.67mm x
1.34mm x
2mm

Row 1: SWI, T1map, PSD map, T1WE, MP-RAGE T1W – 41 year old male healthy control subject scanned with double-echo STAGE at 3T
 Row 2: tSWI, PSDW, actual PSD, simulated T2, T2W – 64 slices for whole brain coverage
 Row 3: iSWIM, R2*, DIR, simulated FLAIR, actual FLAIR – First column MIPs are over 8 slices with effective thickness of 16 mm.

EXTENDED STAGE IMAGING: ADDING DWI AND FLAIR



Clinically DWI and ADC are important images for the physicians particularly in stroke.
Both 3D FLAIR provides the best SNR and CNR for visualizing subtle white matter lesions.

Introduction to STAGE B

Research radiologists are in need of:

- a high quality set of data collected in a reasonable period time that provides a powerful conclusion.
- STAGE B consists of a single interleaved sequence that provides for MRA, MRV, SWI and QSM/SWIM in 5 minutes.

HR QSM (MIP, effective TH=16mm)

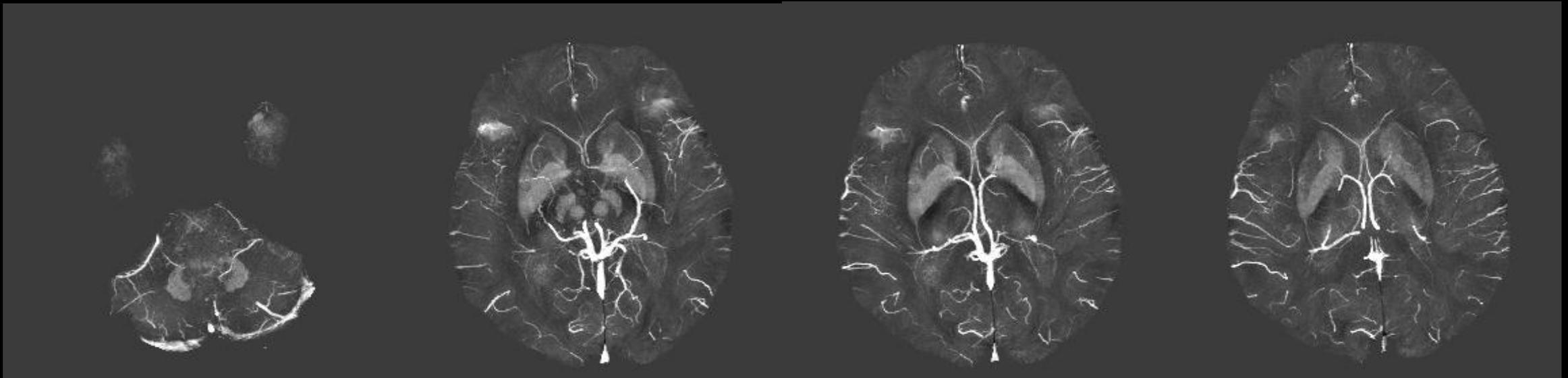
DN

SN

BG

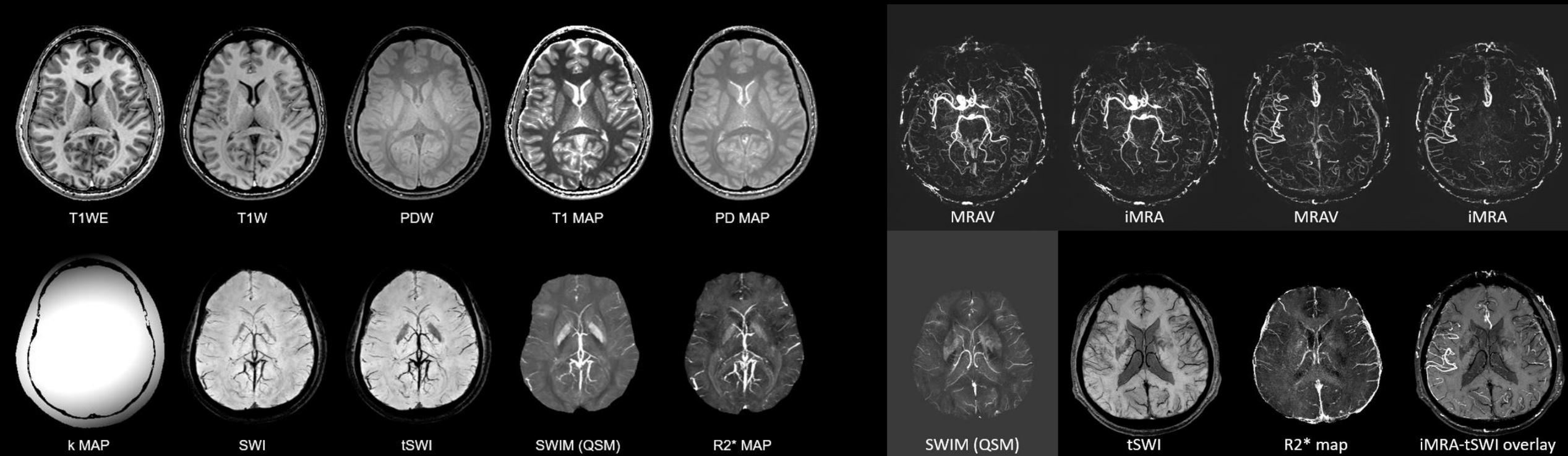
ICV

HR QSM



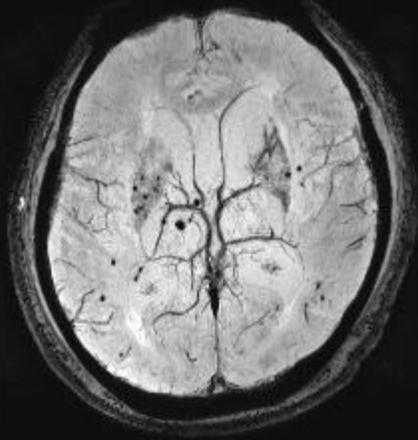
STrategically Acquired Gradient Echo (STAGE) Imaging

STAGE [1-4] is a 5 minute whole brain method that provides a set of multi-echo GRE acquisitions with optimal echo times, flip angles and flow rephasing to obtain multi-contrast qualitative images and quantitative data for studying neurodegenerative diseases. A separate 5 minute MRV scan with specially designed interleaved flow rephasing/dephasing also gives SWI and QSM data.

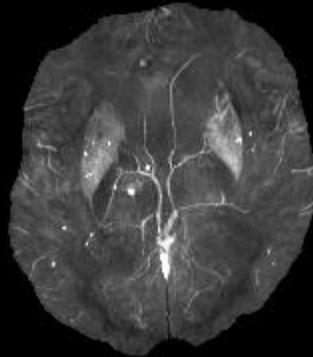


STAGE MRAV: Stroke CMB

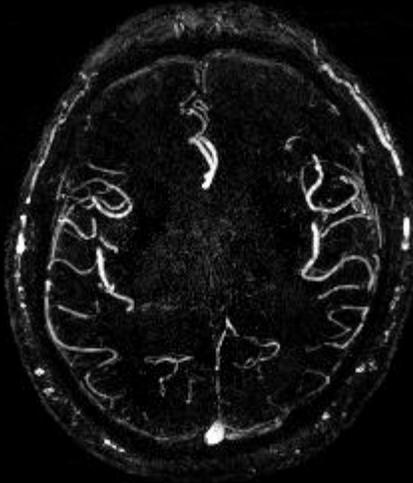
a) SWI



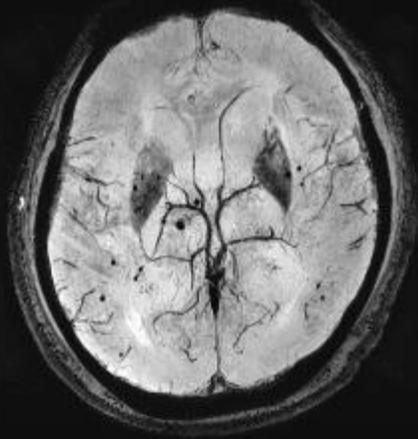
c) QSM/SWIM



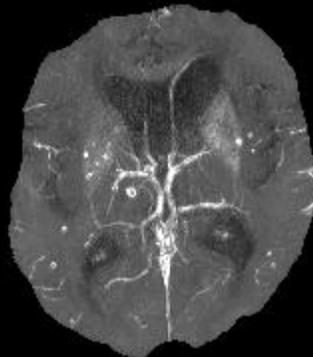
e) MRA



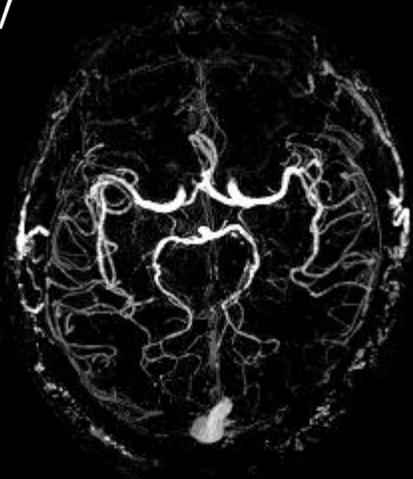
b) tSWI



d) R2*



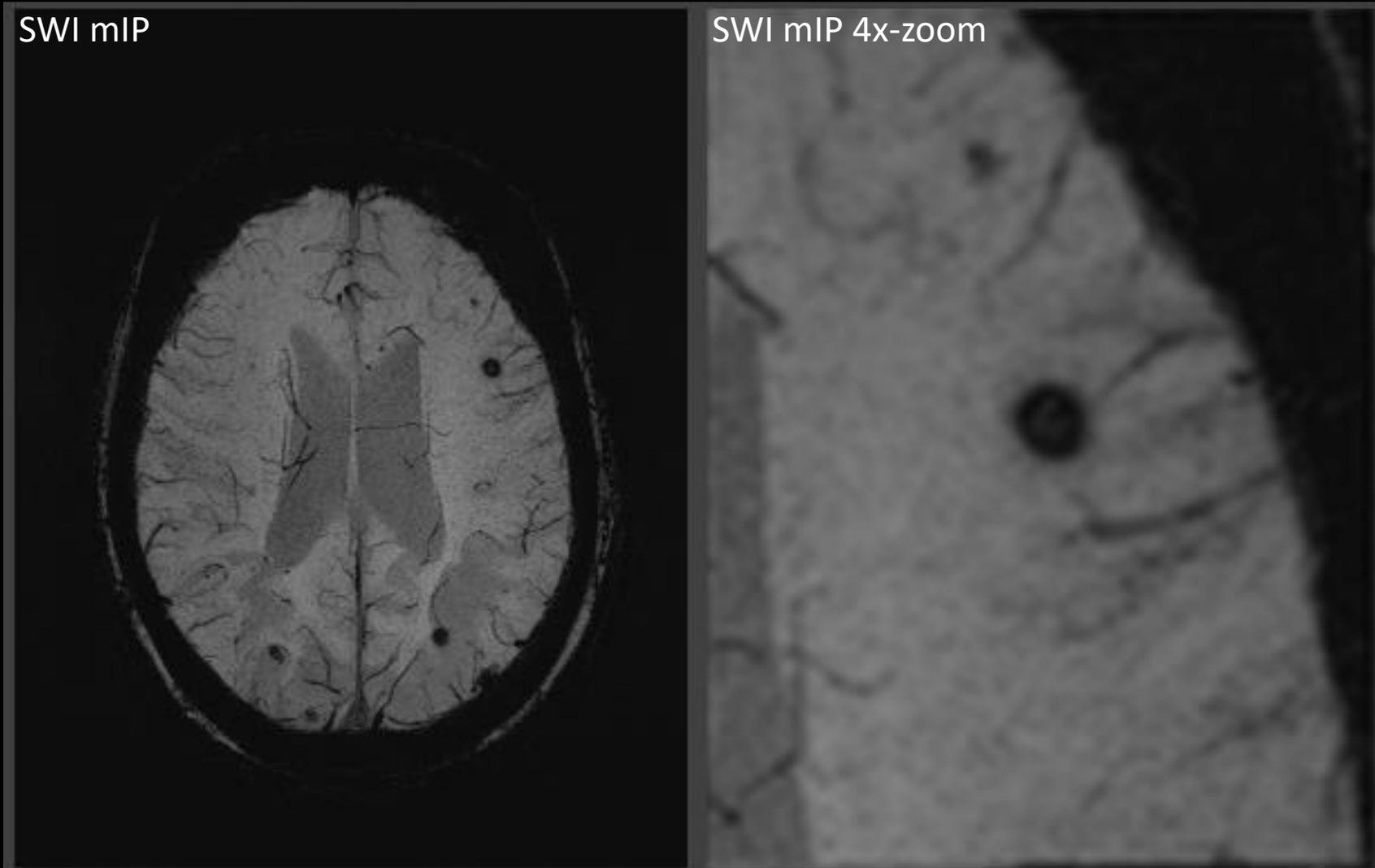
f) MRAV



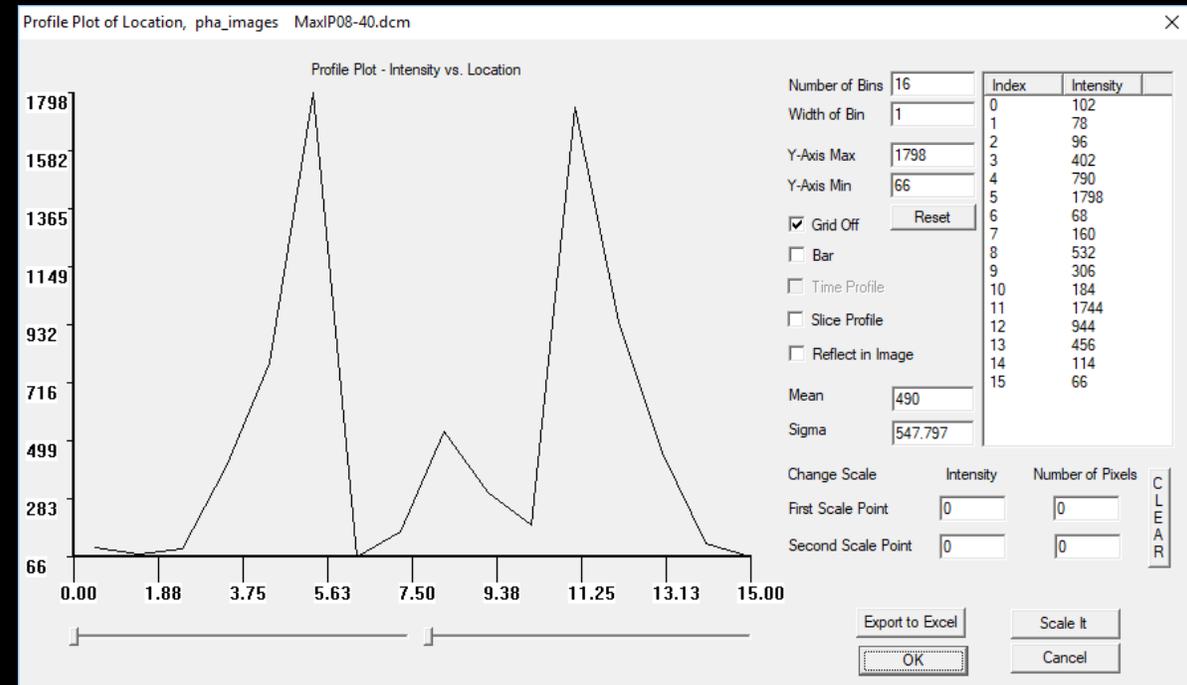
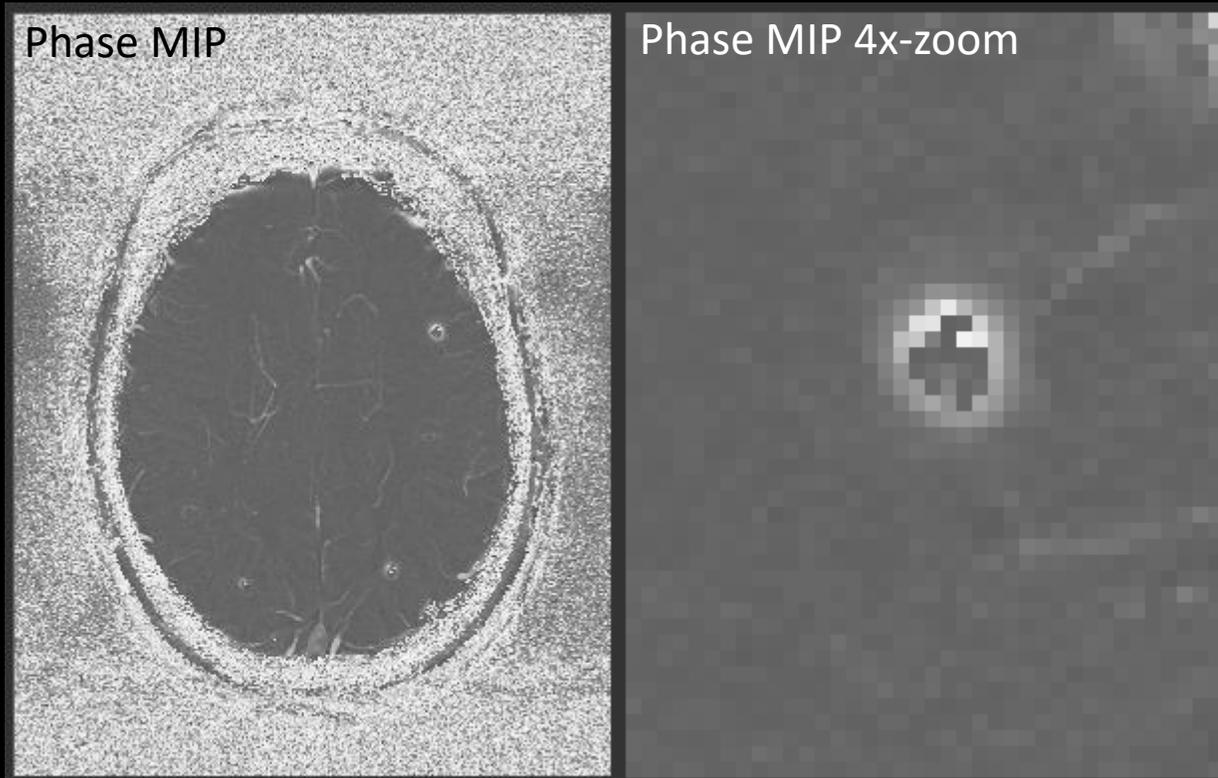
Description of CMB properties

- Sphere or ovoid in shape
- High susceptibility and high R2*
- Lack of connectivity to veins
- Sufficient dephasing for the low FA short echo data

SWI – Are these Hemorrhages in MCI patient?



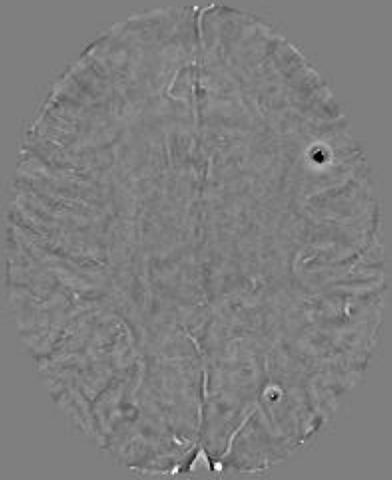
pSWIM – Behaves like Diamagnetic Source



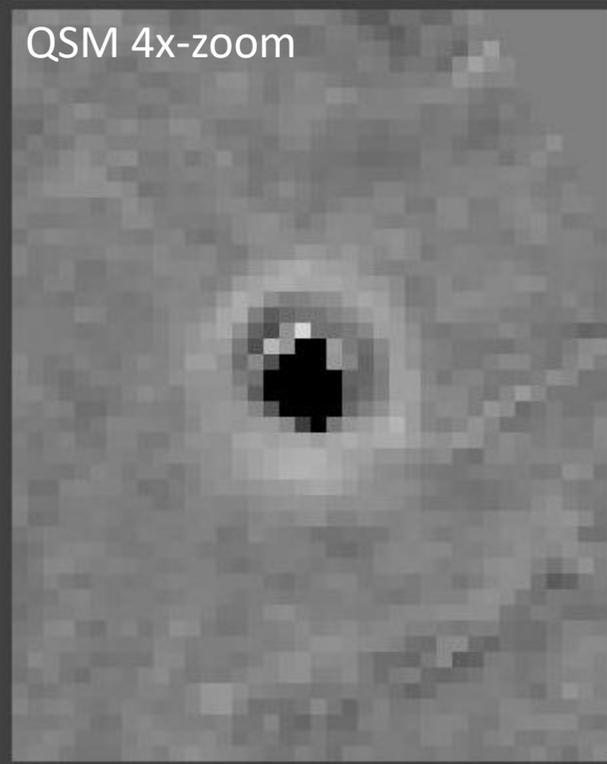
- pSWIM is a Maximum Intensity Projection (MIP) of the SWI filtered phase images.

QSM – Aliasing can be difficult to reconstruct.

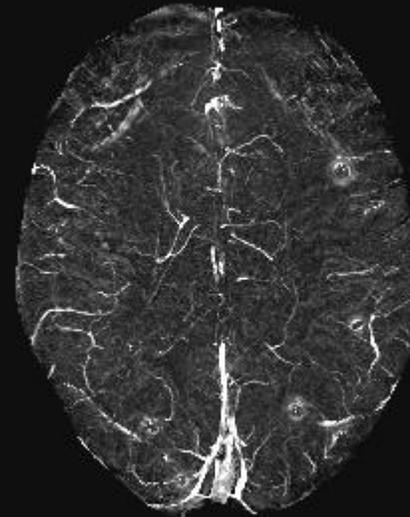
QSM



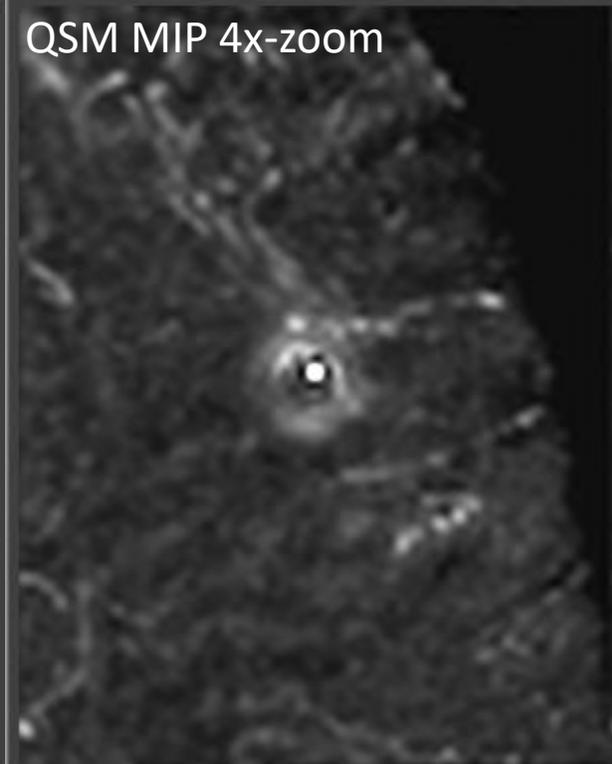
QSM 4x-zoom



QSM MIP

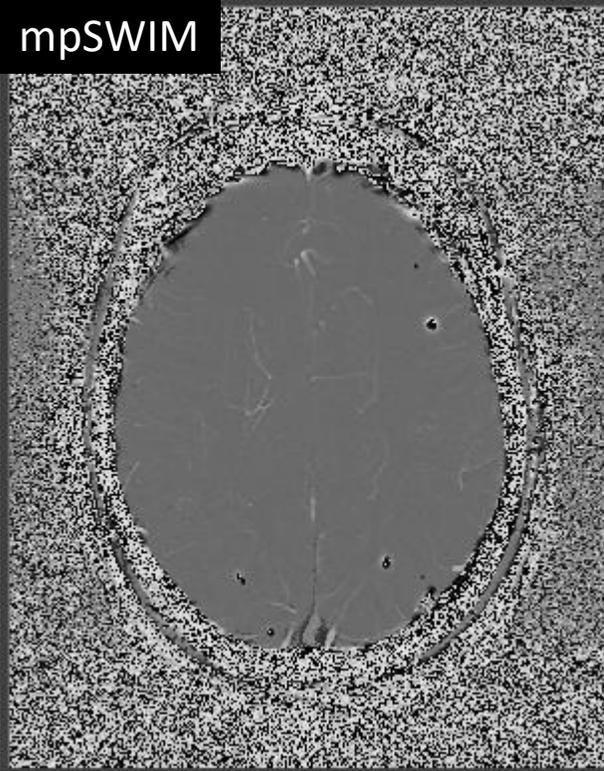


QSM MIP 4x-zoom

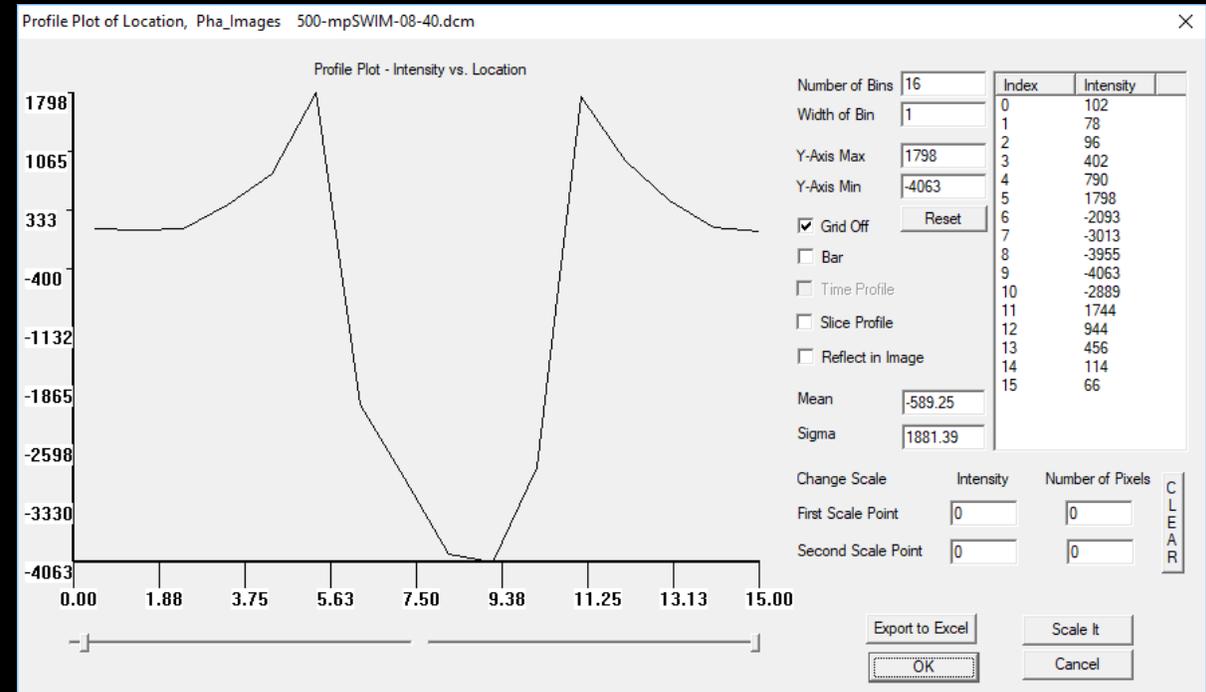
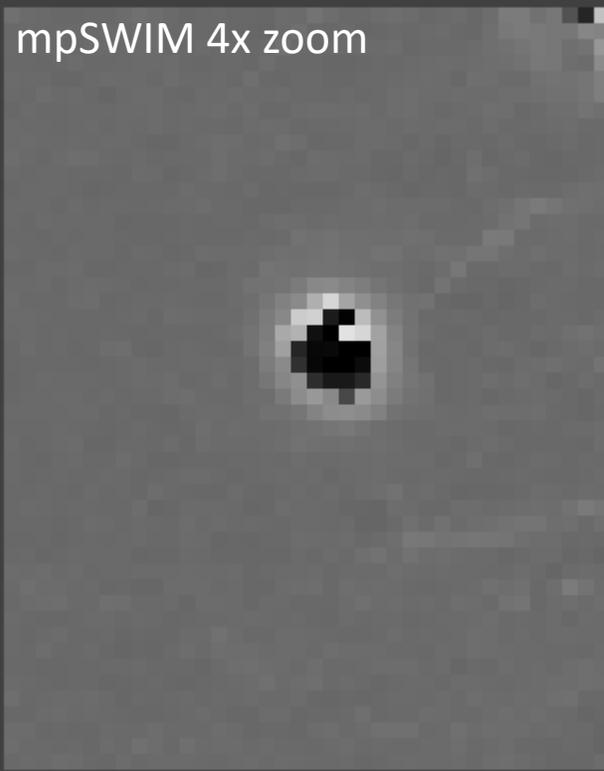


mpSWIM – Confirmed Calcification

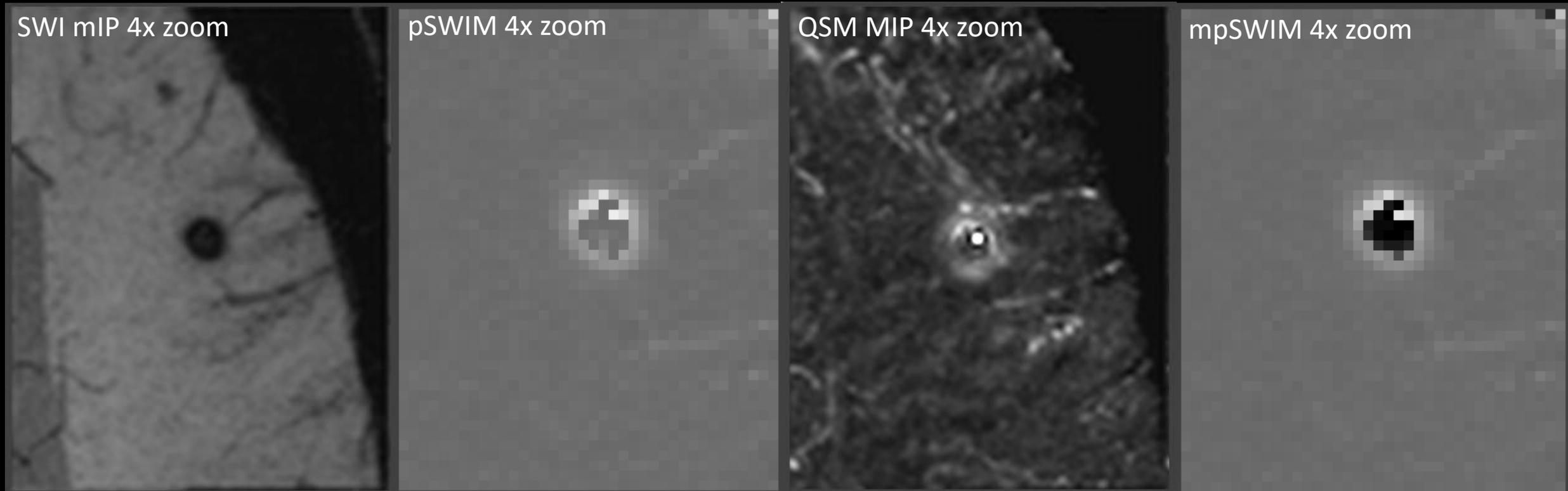
mpSWIM



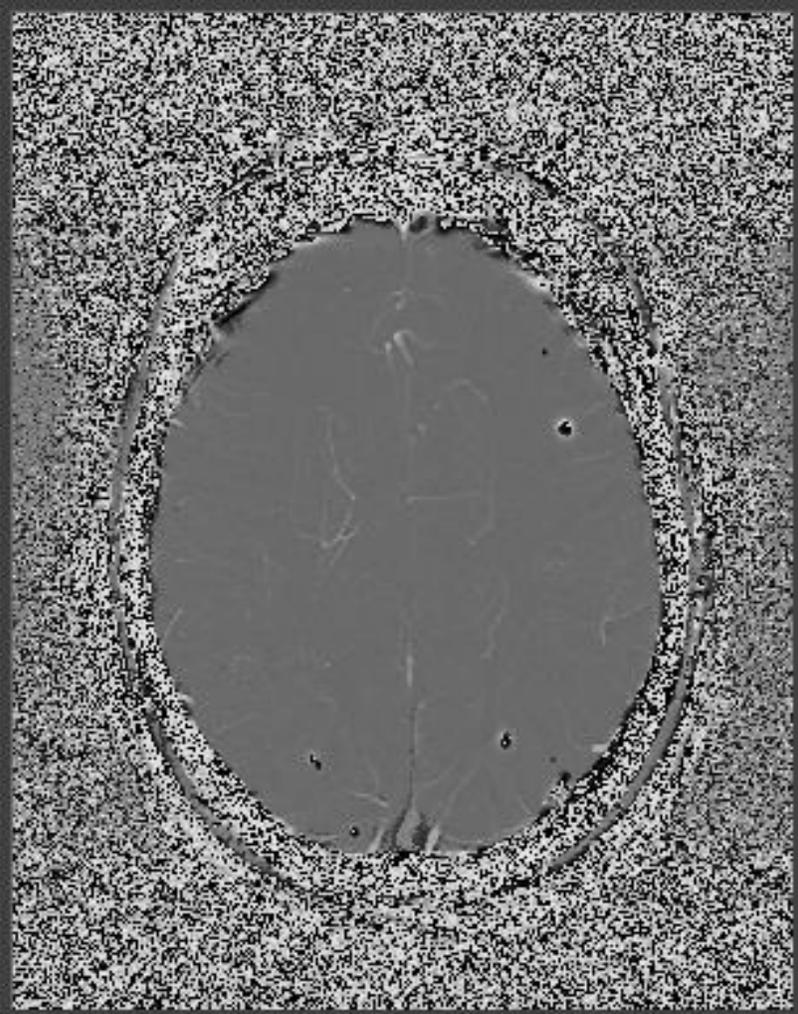
mpSWIM 4x zoom



A straightforward process leads to the same conclusion as a complicated one...

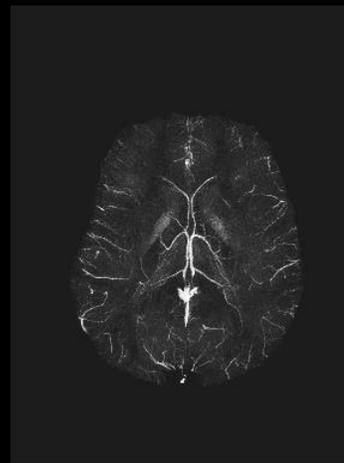
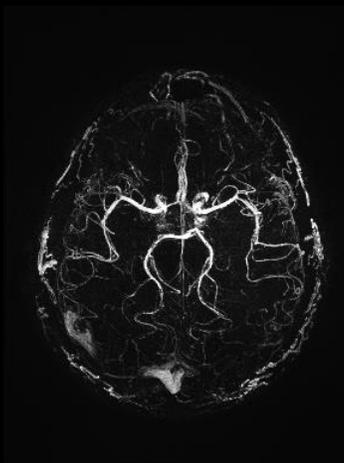


mpSWIM – projection through image slab which depends on the intensity, not an arbitrary preset!



- Intensity in mpSWIM is a maximum intensity projection UNLESS the adjacent intensity is highly diamagnetic.
- Prevents misclassification of non-hemorrhagic lesions.
- Avoids potential artifacts and loss of information due to over processing images. i.e. BET erosion, undulations, aliasing.

THANK YOU FOR YOUR ATTENTION!



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The MRI Institute for Biomedical Research and
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